13. (Once Amended) The method of claim 6 wherein the providing step includes step of adjusting pH of the single liquid solution to acidity.

14.(Once Amended) The method of claim 13 wherein the providing step includes the step of adjusting the pH to basicity.

15.(Once Amended) The method of claim 6 wherein the single liquid composition is biodergradable and non-toxic.

REMARKS/ARGUMENTS

All claims in this application have been amended and are believed to overcome all of the objections and rejections set forth in the First Office Action. These will be addressed in the order they are set forth in the Office Action.

1. Response to the 35 U.S.C. § 112 first paragraph rejections.

Pages 2-5 of the Office Action are devoted to 35 U.S.C. § 112 first paragraph rejections. Applicant believes that the specifications provide an adequate description for enabling one skilled in the art to make and/or use the invention as originally claimed. However, since there are amendments narrowing the claims, the remarks here will be directed to the claims as amended, in view of § 112 first paragraph.

It is believed that the narrowed scope of the claims find sufficient support in the specifications. Namely, the application provides disclosure of the claimed compositions featuring eight different removing agents on page four (Simple Green, Igepal-360, etc.). Other removing agents are identified elsewhere in the specifications. Applicant also discloses tissue activating agents including metal salts (page nine, specific representative examples thereof), chelators (page ten with specific examples enumerated) and buffers (page ten with specific examples enumerated). Furthermore, the preferred concentrations of these compositions are also listed. The preferred adjustment of pH is discussed throughout the specifications including at pages 4 through 10. Pages 11-12 contain preferred embodiments of the

compositions. Pages 13-15 and 18-24 contain almost thirty compositions exemplifying the invention as claimed including how each of these compositions performed in subsequent staining of slides. Experiment 1 on page 13-14 sets forth the specific preparation of the tissue enhancing composition.

Contrary to the Examiner's position stated at page three, lines 14-17, Applicant does disclose numerous compositions, trials and tests which illustrate and predict the effectiveness of the use of an emulsifier and a tissue enhancing agent in an antigen retreival solution to restore antigenicity to formalin fixed, paraffin embedded slides.

The Examiner's position is that it is notoriously well known that hot water melts paraffin. But hot water alone does not emulsify, and while heat may enhance emulsification, heat and water do not produce emulsification of paraffin. It is in emulsification, not melting, that Applicant achieves the composition and methods as claimed. Experimental control is referred to in the specifications on page eighteen (middle of the page).

With regard to the Examiner's arguments on page four, first full paragraph, Applicant's use of salts as tissue enhancing agents do not appear to materially affect the action of the emulsification agent. Applicant does not need to prove how it works, only that it does (see the table on pages 16-18 listing the relative effectiveness of the various compositions). See *Cross v. Iizuka*, 224 U.S.P.Q. 739 (CAFC 1985).

As to the second full paragraph of the Office Action on page four, the claims have been amended to specify paraffin as the embedding medium (paragraph two, page four) and claims 6-16 have been amended to reflect immunohistological staining (paragraph three, page four of the Office Action).

Page five of the Office Action, first full paragraph, Applicant has amended the specifications (see (5) above) to conform to the claims, adding the language "up to 25% by volume of surfactants." The specifications now are sufficient to support claims 2 through 4. The surfactants other than Simple Green are disclosed in various concentrations. Therefore, this rejection is believed to be obviated.

The amendments of the claims have been made to overcome all of § 112 paragraph

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amendments.

Please consider the remarks below in view of the amendments to the specifications and claims. The remarks below are directed to the §§ 102 and 103 rejections set forth in the Office Action.

Claim 1 stands rejected under 35 U.S.C. § 102b as being anticipated by Shi et al (WO 94/04906) ("Shi Patent"). The claim as amended no longer covers solvents or anything else except emulsification agents as the removing agent. The Shi Patent discloses a solvent for dissolving the embedding medium and does not disclose or suggest an emulsifier. The disclosed solvents include alcohols such as ethanol, methanol, propenol, butanol, ethylene glycol and glycerol. These are not emulsifiers and their use promotes dissolving, not emulsification. Furthermore, Shi teaches a two-step process, the first step dissolving and second physically distinct of step of contacting the slide and the tissue with an aldehyde releasing agent. Applicant teaches his single step process using emulsifiers, not solvents.

As to the Thorne reference, it is not believed that this is a proper § 102 reference, Thorne being cited under 35 U.S.C. § 102b. Typically, a § 102 reference must be an enabling disclosure of all elements of the claimed invention without reference to any other art. Nonetheless, it is believed that the partially closed ended language of Claim 1 as amended overcomes this citation. The Thorne disclosure of the urea and Polymyxin B will be destructive to the cell membrane and disruptive to the morphology of the cell-both of which could inhibit the accuracy of post-treatment staining. The action of either or both of such reagents would be detrimental to the later ability of the solved stain to disclose the original morphological characteristics of the cell, defeating the purpose of Applicants compositions and methods.

We turn now to the § 103 rejections beginning at the top of page ten of the Office Action.

I will discuss the disclosure of each of the references, but note at the outset that none of the references disclose a single step process combining dewaxing and antigen retrieval. They all disclose a two step process. A first step of dewaxing and a second step achieving the retrieval of antigenicity. None of the disclosures disclose a single composition having the combination of an emulsifying agent and an antigen

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retrieval (tissue enhancing) composition.

The Hazelbag reference discloses using an "antigen retrieval fluid" on a dewaxed, rehydrated tissue section (page 430 of the reference). This teaches away from the method of wax removal, antigenicity retreval and hydration in a single step.

Several pages of the Office Action discuss the relevant importance of pH and heat on the retrieval of antigenicity. Applicant does not dispute this. However, the prior art also emphasizes that other compositions can help achieve antigenicity retrieval – they are sometimes called "cofactors." Furthermore, it is not in pH adjustment and heat adjustment that Applicant predicates novelty, it is, in part, in pH and heat adjustment combined with the novel emulsification composition and the novel single step method. Hazelbag does not disclose in a single step wax removal, rehydration, and antigen retrieval as set forth in Claims 6-16. Hazelbag teaches away from that in teaching two steps – and perhaps a third (rehydration, it is not clear from the reference), nor is the single combination of Claim 1 disclosed or suggested by any of the four "antigen retrieval fluids" found in the fourth paragraph of page 430 of the Hazelbag reference.

Nor is there motivation to combine Shi (solvents in a two step process) and Hazelbag (variety of compositions in a two step process). They both teach away from the method claims. They both teach dewaxing prior to treatment with an AR solution. There is no suggestion in either to perform a one step process as set forth in Claims 6-16. Nor is there motivation to combine a removing agent with an unmasking agent. Nor is the emulsifier recognized as a removing agent in any reference as cited by the Examiner or known to Applicant.

The Norton reference again notes the use of dewaxed slides (page 371, second full paragraph). Nothing is added, relevant to the single step method or the emulsifier composition than is found in the prior citations. No emulsifier is disclosed in Norton. Miller adds nothing to the prior art, again using dewaxed, rehydrated slides (page 191). No emulsifiers are used or disclosed. Lastly, it is respectfully submitted that the Ding patent reference (eyedrop solutions) and the Prieto patent reference (a laundry detergent) are non-

analogous.

Attached hereto is a mark-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

In view of the above, Applicant respectfully requests the reconsideration.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited on the date shown below with the United States Postal Service in an envelope addressed to the "Commissioner of Patents and Trademarks, Washington, D.C. 20231", as follows:

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Nora B. Aghassi Kim Franceschini Paul J. Ardi SERIAL NO. 09/515,283 FILED: February 29, 2000 TITLE: **COMPOSITION AND METHOD FOR TREATING TISSUE SAMPLES**	ATTY DKT NO. P-6335.01(cip)
TO: Commissioner of Patents and Trademarks Washington, D.C. 20231	

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Attached hereto as Exhibit "A" is a marked-up version of the changes made to the specifications and claims by the current amendment.

Respectfully submitted,

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